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**METHOD FOR IMPROVING
THE PERFORMANCE OF
ELECTROKINETIC MICROPUMPS**

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CERTIFICATION UNDER 37 CFR 1.10

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METHOD FOR IMPROVING THE PERFORMANCE OF ELECTROKINETIC MICROPUMPS

CROSS-REFERENCE TO RELATED APPLICATIONS

5 Not applicable.

STATEMENT OF GOVERNMENT INTEREST

This invention was made with Government support under contract no. DE - AC04 - 94AL85000 awarded by the U. S. Department of Energy to Sandia Corporation. The
10 Government has certain rights in the invention.

FIELD OF THE INVENTION

This invention is directed to a method for increasing the performance of electrokinetic pumps by the use of additives, in the form of zwitterions, to the
15 pumping fluid.

BACKGROUND OF THE INVENTION

Micro Total-Analysis Systems (μ TAS) have received a great deal of recent attention owing to their ability to improve the performance of chemical analysis systems by
20 reducing footprint, reagent volumes, and electrical power needs. As a crucial component of μ TAS research, micropumps have been investigated as a means to move fluids and actuate microscale mechanical components. Electrokinetic micropumps (EK pumps) have been shown to
25 generate pressures above 8000 psi or flow rates above 1 μ l/min, making them attractive for miniaturization of HPLC systems (cf. U.S. Patent No. 6,277,257

"Electrokinetic High Pressure Hydraulic System"), cooling of microelectronics, and actuation of microscale mechanical components. Thus, EK pumps are ideally suited for micro total-analysis systems since they can
5 straightforwardly meter the very low flow rates (nl/min or μ l/min) that are typically used, and can generate high pressure (thousands of psi) required for chromatographic separations.

An EK pump uses electroosmosis in charged porous
10 media to generate a pumping function and is realized experimentally by applying voltage across a porous bed possessing a charged-solid-liquid interface, as shown in FIG. 1. Electroosmosis due to the applied electrical field causes fluid flow and generates a pressure whose
15 magnitude depends on the Darcy permeability of the fluidic channels downstream of the pump. Pump performance is dictated by substrate material and geometry as well as fluid properties. In order to facilitate miniaturization of μ TAS and microfluidically
20 driven systems generally it is desirable to incorporate improvements that lead to reduction in voltage and power requirements and improved fluid flow rates.

SUMMARY OF THE INVENTION

Accordingly, the present invention is directed
25 generally to improving the performance of electrokinetic (EK) pumps through the use of zwitterion additives in the pumped fluid.

The permittivity or dielectric constant (ϵ) of a pumping fluid is a fundamental performance parameter of an EK pump system. For maximum pressure performance ϵ should be maximized. Since ϵ is a strong function of solute concentration, increases in solute concentration should have a beneficial effect on ϵ and pressure performance of an EK pump. Charged solutes, such as NaCl cause a decrease in permittivity of water and lead to undesirable increase in conductivity and joule heating. However, chemical compounds such as zwitterions when dissolved in the pumped fluid influence EK pump performance by increasing permittivity ϵ without increasing fluid conductivity. In fact, net neutral zwitterions typically reduce conductivity to additional benefit. The use of these chemical compounds as additives to EK pump fluids has been shown to result in a 3-fold increase in pump efficiency and a 2.5-fold increase in generated pressure for a given applied voltage.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic illustration of a generic electrokinetic pump.

Figure 2 shows the pressure/volt plotted as a function of the TMAPS additive concentration.

Figure 3 shows EK pump efficiency as a function of solute concentration.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, it has been discovered that the use of a class of additives, generally comprising zwitterions, which when added to the pump fluid, or electrolyte, improve the pumping performance of electrokinetic pumps by increasing the maximum pressure and flow rate generated as well as the maximum efficiency for a given applied voltage.

In order to understand the present invention better, the following introductory discussion is provided. An electrokinetic pump comprises an apparatus for converting electric potential to hydraulic force. Referring now to FIG. 1, an electrokinetic pump or EKP typically consists of at least one duct or channel that can be a capillary channel or microchannel, that forms a fluid passageway having an inlet and an outlet. The capillary duct or channel contains an electrolyte and has a porous stationary phase or substrate comprising a nonporous dielectric medium disposed therein between one or more pairs of spaced electrodes. Porous dielectric medium can include small particles, high surface area structures fabricated within the microchannel, or microporous materials such as monolithic polymer networks (cf. U.S. Patent Application No. 09/796,762 "Castable Three-dimensional Stationary Phase for Electric Field-driven Applications"). An electric potential is applied

between electrodes **130** in contact with electrolyte, or pump fluid, **115**, that can be an aqueous or an organic liquid or mixtures thereof, to cause the electrolyte to move in the microchannel by electroosmotic flow and
5 generate a pressure whose magnitude depends on the Darcy permeability of the fluidic channels downstream of the pump. Pump performance in terms of pressure generated per volt of applied electric potential is determined by composition of the porous dielectric material or
10 substrate material and geometry as well as the properties of the electrolyte. Throughout the written description of the invention the terms "electrolyte" and "pump fluid" will be used interchangeably and synonymously.

15 At the interface between a charged solid and an electrolyte solution and electrochemical double layer is formed and the mobile (diffuse) component of the double layer moves in response to the force generated by an externally applied electric field giving rise to
20 electroosmotic flow. Assuming a cylindrical capillary geometry with radius a and phenomenological zeta potential ζ as well as a liquid with viscosity μ and permittivity ϵ , Poisson's charge density equation and Stokes' flow equations can be combined to give the
25 electroosmotic flow profile as

$$(1) \quad u(r) = \frac{P_x}{4\mu}(a^2 - r^2) - \frac{\epsilon\zeta E}{\mu}$$

where P_x is the pressure gradient along the axis, r is the radial position, and E is the uniform electrical field. Equation 1 can be used to derive a number of performance relations for EK pumps that consist of linear capillaries and operate in the thin-double-layer limit. Practical EK pumps consist not of linear capillaries but rather a porous bed; Equation 1 can thus quantitatively treat porous media only if additional parameters (e.g., formation factors, porosity, tortuosity) are used to adapt the microchannel geometry to that of the porous bed. These additional parameters add multiplicative factors to Equation 1 and the derived results to follow. However, we are concerned primarily with the relative performance increase observed upon addition of specific fluid additives, thus the treatment for an idealized linear capillary system will be retained; it is simple and sufficient for this purpose.

From Equation 1 we can derive that the maximum pressure per volt generated in such a capillary (i.e., the pressure performance at zero net flow rate) is

$$(2) \quad \frac{\Delta P_{\max}}{V} = \frac{8\epsilon\zeta}{a^2}$$

where V is the applied voltage. As a practical example, we can use Equation 2 to estimate that for a packed bed of 0.5 μm silica beads (effective pore radius $a \approx 100$ nm) and an electrolyte fluid consisting of a 10mM aqueous
 5 Tris [Tris-(hydroxymethyl)aminomethane hydrochloride] buffer ($\zeta \sim 60$ mV), the maximum pressure achieved will be 4.9 psi/volt.

Expanding the microchannel model to consider an array of identical microchannels of length l and total
 10 open cross-sectional area A , the maximum flow rate generated per applied volt can be derived as

$$(3) \quad \frac{Q_{\max}}{V} = \frac{\epsilon \zeta A}{\mu l}$$

15 Returning to the packed silica bead example and assuming the beads are packed into a 150 μm diameter cylindrical porous bed with a porosity of 0.33 and length of 5 cm, Equation (3) gives $Q_{\max}/V = 0.3 \mu\text{l}/\text{min}/\text{kV}$.

Since this flow is in the Stokes regime, the system
 20 is linear and a straightforward relationship for the flow rate or generated pressure can be derived from Equations 2 and 3:

$$(4) \quad Q = Q_{\max} \left(\frac{\Delta P_{\max} - \Delta P}{\Delta P_{\max}} \right)$$

Finally, we can define the efficiency as

$$(5) \quad \eta = \frac{Q\Delta P}{VI}$$

5

where VI is the applied electrical power and $Q\Delta P$ is the generated mechanical power. Thus, for a given value of applied electric power, the higher the efficiency the greater the generated mechanical power. Here we have
10 tacitly ignored the convective contribution to the charge transport, an assumption that is typically valid only at high ionic strength. Differentiating Equation (5) and inserting Equation (4) leads to the conclusion that maximum efficiency is achieved at $P=0.5P_{max}$.

15 From Equations 2-5, design requirements for the substrate material, substrate porosity, solvent fluid, and dissolved species in the thin double layer limit are clear. The substrate material affects the zeta potential ζ , and maximizing ζ will maximize pressure,
20 flow rate, and performance. Silica surfaces have high wall ζ potentials at neutral pH and above, and are a common material choice. Choice of pore size directly affects pressure performance but does not affect flow rate. Solvents should be chosen to maximize
25 permittivity and minimize viscosity. Water has typically been an attractive fluid for high-pressure

applications, due to its high permittivity ($\epsilon \sim 81$, $\mu = 1$
mPa s at room temperature), while the addition of
acetonitrile to aqueous pump fluids increases pumping
rates, since its permittivity and viscosity ($\epsilon \sim 37$,
5 $\mu = 0.37$ mPa s) lead to a slightly better ϵ/μ ratio.

A minimum buffer concentration is often necessary
for chemical analysis or synthesis. Here we assume that
a nominal buffer concentration is required, and that
that concentration leads to thin double layers. In this
10 limit, addition of further charged species increases
conductivity and power dissipation in the fluid,
reducing efficiency and increasing unwanted thermal
effects. Added counterions also reduce the zeta
potential. Hence, in the thin double layer limit,
15 efficiency is inversely proportional to concentration of
charged species.

While uncharged solute additives do not
significantly affect conductivity, double layer
thickness, wall zeta potential, or pH, they can have a
20 large impact on the permittivity and viscosity of the
solution. In general, the permittivity of a dielectric
electrolyte solution can be approximated using a linear
dielectric increment $d\epsilon/dC$:

25 (6) $\epsilon(C) = \epsilon(0) + \frac{d\epsilon}{dC} C$

where C is the concentration of solute and the linear dielectric increment is a property of the specific solute-solvent system. Normalizing these values, we can write

5

$$(7) \quad \varepsilon^* = 1 + \gamma_\varepsilon C$$

where $\varepsilon^* = \varepsilon / \varepsilon(0)$ and $\gamma_\varepsilon = d\varepsilon / dC / \varepsilon(0)$. Equation 6 is rigorously valid only for infinitesimal concentrations but is typically accurate for practical concentrations, and will be shown below to be applicable up to concentrations as high as 2.5 M for some additives.

Upon addition of an uncharged additive, the electroosmotic flow velocity scales with the permittivity change, leading to a change in pressure performance:

15

$$(9) \quad \frac{P_{\max} / V}{(P_{\max} / V)_0} = 1 + \gamma_\varepsilon C$$

Here and in the following equations, the subscript 0 denotes the value at zero concentration. The change in EOF velocity similarly affects flow, but is offset by changes in the fluid viscosity:

$$(10) \quad \frac{Q_{\max}/V}{(Q_{\max}/V)_0} = \frac{1 + \gamma_e C}{\mu^*}$$

where $\mu^* = \mu/\mu(0)$ is the normalized viscosity whose functional form is left unspecified. Pressure and flow effects combine to give the efficiency:

$$(11) \quad \frac{\eta}{\eta_0} = \frac{(1 + \gamma_e C)^2}{\mu}$$

From Equations 9-11, it is clear that chemical compounds with large γ_e e. g., large dipole moment, can greatly enhance EK pump performance as additives to the electrolyte. From the discussion above, it is also clear that it is desirable that the additives be uncharged. Such a class of chemical additives is characterized and represented by the genus zwitterions.

Zwitterions comprise a class of molecules that contain separated positive and negative charge centers within the molecule, are substantially electrically neutral, and generally exhibit a large inherent dipole moment (≈ 20 -25 D) as a consequence of charge separation within the structure of the molecule. Positive charges can arise from one or more groups within the molecule including primary amine, secondary amine, tertiary amine, or quaternary amine. Negative charges can arise

from one or more of the groups including sulfonate, phosphate, carbonate, or carboxylate.

The dielectric increment ($d\epsilon/dC$) of zwitterions stems primarily from the additive effect of their dipole moments to the inherent dipole moment of the solvent. Many families of zwitterions (e.g., trialkyl ammonium alkane sulfonates, alkyl imidazole alkane sulfonates, alkyl pyridine alkane sulfonates) have large positive dielectric increments ($>40/M$) in water, and are readily soluble in water such that solution concentrations above 1 M can be prepared. When added to aqueous pump solutions, zwitterions lead to large permittivity increases and thus provide for improved pump efficiency, pressure, and flow.

In the example below, the improvement in EK pump performance, namely increased maximum pressure generated per volt of applied electric potential and improved efficiency, realized by adding the zwitterion trimethyl ammonium propane sulfonate (TMAPS) to the EK pump fluid is demonstrated. TMAPS was chosen both for its high dielectric increment as well as commercial availability. TMAPS is known to have a $d\epsilon/dC$ of $+52/M$, is uncharged at neutral pH, and is soluble to 3.5 M.

While one aspect of the invention will be illustrated by the example below this example only serves to illustrate the invention and is not intended to be limiting. Modifications and variations may become

apparent to those skilled in the art, however these modifications and variations come within the scope of the appended claims. Only the scope and content of the claims limit the invention.

5

EXAMPLE

Electrokinetic pumps similar to that shown in FIG. 1 were prepared. Porous stationary phase **120** was 0.5 or 1.0 μm nonporous silica microspheres. The inlet end of the pump was immersed in the running solution and voltage was applied by a high-voltage power supply. The high-pressure end of the pump was electrically grounded and connected through the pump fluid to both a pressure transducer and an outlet with controlled Darcy permeability (infinite for P_{max}/V measurements, zero for Q_{max}/V measurements, approximately the permeability of the pump for η measurements). Pressure was given by the transducer output, and flow rate was calculated from microscopic observation of the motion of the liquid-air meniscus in a 149 μm ID capillary. Voltage and current were monitored using an electrometer, and a computer was used to acquire data.

Solution viscosities, necessary to predict flow rate performance, were inferred by using a syringe pump to induce a controlled 12.5 $\mu\text{l}/\text{min}$ flow rate through a 1 m length of 150 μm ID capillary and observing the upstream pressure.

The effect of TMAPS on pump performance was

evaluated by measuring flow, pressure, and efficiency of two EK pumps with solutions with varying TMAPS concentrations. One pump, denoted as pump A, was a 150 μm diameter capillary packed with 1 μm silica beads; the
5 second pump is denoted as pump B and consisted of a 100 μm diameter capillary packed with 0.5 μm silica beads.

The maximum-pressure performance of the pump was measured by sealing the pump outlet to produce zero net mass flux through the pump. The effect of TMAPS was
10 observed by measuring P_{max}/V for various TMAPS concentrations in 10 mM pH 8 Tris buffers. At each concentration, equilibrium pressure was recorded as a function of several applied voltages, and the observed pressure vs. voltage curve was fit to a linear
15 relationship, whose slope gives the pressure/volt parameter from Equation 2. FIG. 2 shows the pressure/volt response normalized by the value observed without TMAPS, plotted as a function of the TMAPS additive concentration. Error bars indicate the
20 standard deviation of the linear fit. The TMAPS additive caused up to a 2.5-fold increase in the observed P_{max}/V over the Tris buffer alone, leading to P_{max}/V results as high as 22 psi/V. The increase was linear up to 2.5 M TMAPS, and is consistent (RMS error
25 8%) with a prediction using a linear model for dielectric constant (Equation 9). A least squares fit of the 0-2.5 M region gives an inferred dielectric

increment of 47.6/M, which is in agreement with a reported value of 52/M for TMAPS (Lucy, C. A.; Woodland, M. A., Stockholm, Sweden 2002; The Swedish Chemical Society Analytical Division.) and is consistent with the
5 value of 42.2/M reported for a similar compound, triethylammonium propane sulfonate. (Galin, M.; Chapoton, A.; Galin, J. C. *Journal of the Chemical Society, Perkin Transactions 2* **1993**, 3, 545-553.)

From FIG. 2, we can also observe that while
10 variation in fabrication can lead to changes in the absolute performance of individual pumps, these variations do not affect the relative impact of solute additives on performance.

Efficiency was calculated from pressure, flow,
15 voltage, and current observations and the results are displayed in FIG. 3. Pump A was evaluated at $P=0.47P_{max}$ ($\eta=0.996\eta_{max}$), and pump B was evaluated at $P=0.65P_{max}$ ($\eta=0.91\eta_{max}$). The prediction of Equation 11 is shown for comparison. The addition of TMAPS increased the
20 efficiency of the pump in the 0-2.5M TMAPS range. Equation 11 predicts a maximum efficiency at 1.6 M TMAPS, at which point the efficiency has increased by 2.2. The maximum increase in efficiency was seen at 2.5 M TMAPS, where the pump was 3.2 times as efficient as
25 compared to Tris alone as the fluid. The maximum observed thermodynamic efficiency was obtained with pump B at 2.5 M TMAPS, an efficiency of 5.6%.

As shown in the example above, the permittivity increase caused by zwitterion additives will significantly improve pump and actuator performance. The increase will allow the μ TAS designer greater
5 freedom in device construction. For a given pressure or flow requirement, improved pump performance implies that smaller voltages may be used, reducing substrate voltage holdoff requirements, electrolysis and bubble
10 high-voltage board performance requirements. For a given voltage, increased pressure improves chromatographic performance while increased flow improves the temporal response of EK-pump-driven actuators.